DEPARTMENTS

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A think tank for health, right in the Burgh.
An answer for pilfered X rays.
Mutual respect: MAA award winners.

INVESTIGATIONS
Pitt tries on Eastern traditions.
When napping is not enough, a gene linked to preeclampsia may be key.
Tracking HIV transmission.

ATTENDING
Who gets into the School of Medicine and why? Lurk around an admissions committee session.

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Find out who’s coming to your neighborhood.

98.6 DEGrees
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ALUMNI NEWS
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COVER STORY
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The Manhattan Project, the polio vaccine, an antiviral to halt any possible future influenza pandemics—Julius Youngner is always in the middle of “the next big thing.”
BY REBECCA SKLOOT

FEATURES
Quick on Their Feet
What do you do if you’re a medical student and your country’s naval base is bombed? According to alumni from the ’40s, you learn how to become a doctor, fast.
BY EDWIN KIESTER JR.

When Light Bends Back on Itself
Now if we pump the rays just right, we’ll see what this tissue looks like at half a micron. Simon Watkins’s magical view of life.
BY PATRICIA M. PARK AND ERICA LLOYD

Precious Cargo
One out of every six gene therapy trials conducted to date has taken place at Pitt. The school is a national center for one of today’s most earth shaking, and now highly scrutinized, therapies.
BY REBECCA SKLOOT

CONTRIBUTORS
EDWIN KIESTER JR — [*Quick on Their Feet*] Edwin Kiester (CAS ’50) was an undergraduate watching Pitt medical students march across campus in 1944 before donning a uniform himself. He is a California-based freelance writer whose work has appeared in Smithsonian, Reader’s Digest, and many other magazines.

JIM JUDKIS — [Cover and “To Stop Death in Its Tracks”] Jim Judkis lives in Franklin Park, Pennsylvania. He’s known for his environmental portraiture; in addition his work can be found in 15 children’s books.

COVER
Julius Youngner’s latest project may save us all. (Photo by Jim Judkis.)
n May, I had the pleasure of leading graduation ceremonies for the School of Medicine Class of 2000. And what a class it was! These students came to us as former college athletes, attorneys, classical—and not so classical—musicians, and teachers. One each was an air force officer, Peace Corps volunteer, and ballerina. Their diversity of backgrounds and interests symbolizes, and will surely influence, the diversity of approaches to clinical and research issues that will characterize medicine in this decade and beyond.

The day after graduation, we held our annual Curriculum Colloquium. This is a one-day exegesis and analysis—novel if not rare among medical schools—not just of what we are teaching but how we are teaching. We evaluate our mentoring and use of the Internet to facilitate teaching and learning (not to build bells and whistles just because we can) and critically review didactic material to be sure our lectures don’t belong in the Carnegie Museum’s paleontology collection.

On the curriculum content side, we reinforced the need to keep up with the biology of the human condition as fast as it is being breathtakingly revealed. We have to integrate structural, molecular, developmental, computational, and cellular biology in such a way that students can metabolize this new knowledge as it quickly evolves to form the scientific basis of medicine. But students must also gain clinical and practical skills. Particularly in this day and age, they need to be alert to the cost of the care they provide. They must understand the social, economic, cultural, political, and family context in which illness emerges. And they must be sufficiently conversant in the scientific method to identify the real kernel of new knowledge in the scientific (and often pseudoscientific) chaff.

We invite students to join us for the colloquium—this day of soul-searching—and urge them to tell us what they think about the quality of their mentoring and the relevance of the textual material. They do. We view this process as essential because medical schools exist, after all, to teach students. Unfortunately, the clinical pressures of the managed care vise leave many faculty with less time to teach or to think about how to teach creatively and with passion.

As one way to address this problem, our faculty will get “double mileage” for teaching as of this July. Our internal currency for calculating academic level-of-effort is the educational credit unit. Beginning this fiscal year, all medical school departments will receive twice the funding per faculty teaching unit as they have in previous years. This is just one way in which we can make our reward system synchronous with our value system. I’ll put my money on our students any day.

Arthur S. Levine, MD
Senior Vice Chancellor for the Health Sciences
Dean, School of Medicine
That’s No Mercedes-Benz

For years, pathologists have seen a shape similar to the Mercedes-Benz symbol in cancerous tumor specimens. Pitt researchers Susanne Gollin and William Saunders decided to ask why, and ended up producing the first graphic of how this abnormal, Y-shaped arrangement of chromosomes forms in cancer cells. Gollin, associate professor of otolaryngology and pathology at the School of Medicine (who also is in the department of human genetics at the Graduate School of Public Health), and Saunders, assistant professor of biological sciences, say studying these mechanisms of chromosome missegregation will shed light on the biology of cancer and could eventually lead to a technique to curb cancerous growth. Image "A" shows chromosomes lining up normally across from two spindle poles during normal cell division. Images of cells dividing abnormally (B-E) show how extra poles are generated, it appears, haphazardly. –ET

FOR MORE INFORMATION: http://www.upcl.upmc.edu/internet/cytogen/

FOOTNOTE
“We learned to estimate how soon a baby would come, not by effacement and dilation, but by the pitch of the “Oh, Lordy” and “Oh, Mama.”

—Daniel D. Nixon’s 1959 Class History

RAND/PITT PARTNERSHIP
Better health care for all: It’s no longer a pipe dream, but in the pipeline. The University of Pittsburgh and RAND, a California-based nonprofit think tank, are establishing the RAND/University of Pittsburgh Research Institute here to do more than just ponder and evaluate methods of medical delivery. Researchers will use western Pennsylvania as a real-life laboratory, testing new programs and treatments that could improve health care delivery across the country. Harold Pincus, professor and vice chair of the School of Medicine’s Department of Psychiatry, will direct the new institute.
Faculty Snapshots

Here’s a glimpse of some of the School of Medicine faculty’s intriguing work:

**Bora Baysal and Bernard Devlin**, assistant professors of psychiatry, have linked for the first time flaws that alter mitochondria to genetically inherited cancers. Baysal, Devlin, and fellow researchers found that when a certain tumor thrives in a region of the neck where blood oxygen levels are sensed by cells, it also shuts down the mitochondria’s ability to appropriately detect these levels. These findings were reported in the February 4 issue of *Science*.

**Wendy Rubinstein**, assistant professor of medicine, was a coinvestigator in Baysal and Devlin’s study. She also is heading the Cancer Genetics Program at the University of Pittsburgh Cancer Institute and Magee-Womens Hospital, which offers expert clinical consultation and teaching services and performs research on hereditary cancer.

**Kenneth McCarty**, professor of medicine and pathology, has devised a decision-making instrument that tailors prostate cancer treatments according to a patient’s preferences. Funding for this tool came in part from an $800,000 Commonwealth of Pennsylvania grant to carry out the Comprehensive Prostate Cancer Awareness Program. Recipients include the School of Medicine’s Department of Urology, the University of Pittsburgh Cancer Institute, and UPMC Health System.

**Deborah McMahon**, associate professor of medicine, Pitt Treatment Evaluation Unit (PTEU) medical director, and coinvestigator of the Pittsburgh Adult AIDS Clinical Trials Group, will use a more than $6 million NIH AIDS research grant to expand clinical research and advance the care of HIV-infected individuals in this area.

**Carl Olson**, associate professor of neuroscience and director of the primate physiology lab at the Center for the Neural Basis of Cognition, has pinpointed the location in the brain that accounts for why humans tend to confuse items that are mirror images of each other. When people have trouble recalling if an item pictured was facing left or right, his studies showed that a mechanism in the inferotemporal cortex (IT) triggers electrical activity in an equal number of nerve cells for the mirror image of that picture. Olson’s conclusions were published in *Science* on February 25. —ST

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THE SHOT HEARD ROUND THE WORLD

All those March of Dimes campaigns paid off in 1955. After years of research, Jonas Salk, Julius S. Youngner, Major Byron L. Bennett, L. James Lewis, Percival L. Bazeley, Ulrich Krech, and others in the Virus Research Laboratory at the University of Pittsburgh developed the killed poliovirus vaccine. Media dubbed it “the shot heard round the world.” This April, the School of Pharmacy erected a permanent exhibit on the fourth floor of Salk Hall to commemorate the discovery.

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FOOTNOTE

Pay attention, or don’t. From “The Unofficial Pitt Med School Web Site”: “The PBL [problem-based learning] rooms are only a few years old, so in order to keep them new, we are not allowed to eat in them. If you decide to eat in the PBL rooms (which everyone does), clean up after yourself.”
This year’s Medical Alumni Association award winners couldn’t be more grateful if the School of Medicine had been gift wrapped and delivered to their doorsteps. Both winners—Freddie H. Fu, MD ’77, who received the Philip S. Hench Distinguished Alumnus Award, and Paul B. Nelson, who received the McEllroy Award—share an affinity for the school.

Fu, David Silver Professor and chair of the Department of Orthopaedic Surgery, says of his more than 70 professional awards, the Hench Award means the most.

“This is a very different award. It’s from my fellow alumni, and I feel very privileged,” he says. Fu is team physician for Pitt’s athletic department and in his spare time conducts research in tissue engineering, robot-aided surgery, and nerve function in sports.

Nelson has been chair and Betsy Barton Professor of Neurological Surgery at Indiana University since 1992. Nelson misses Pitt and is grateful for the time spent here; so the McEllroy Award—given to a nonalumnus who did residency training at the University—pleases him as evidence of “mutual respect.”

While in Pittsburgh, Nelson was UPMC Presbyterian medical staff president. At Indiana, he established a spinal cord injury center. He also directs a neurosurgical training program, an opportunity that lured him from Pittsburgh.

“I enjoy patient care and research, but resident education is my true love,” says Nelson. He notes he has worked with previous McEllroy Award recipients.

Both he and Fu are happy to join the ranks of Pitt colleagues who have received the awards.

“This school has grown into a world-class facility,” says Fu.

From Bench to Bedside

In the University of Pittsburgh Cancer Institute outpatient clinic, assistant professor of medicine Adam Brufsky discusses a breast cancer patient’s condition with medical student Shannon Penland, MD ’00. They chat briefly with the fatigued woman, then talk after she leaves Brufsky’s recommended treatment.

Sounds like a typical hands-on experience for a fourth-year student. But Brufsky’s clinic is part of a School of Medicine Integrated Life Sciences (ILS) course on neoplasia, which means that Brufsky and Penland are getting a dose of basic science lectures to take with them to the patient bedside.

Brufsky and Robert Getzenberg, associate professor of medicine, pathology, and pharmacology, organize the neoplasia course, one of four ILS offerings the medical school created in 1995. (The course was originally designed by Candace Johnson of pharmacology.) A fifth course was added two years ago, and a new ILS in neuroscience begins in the fall.

Brufsky gives students a chance to slow down. Instead of seeing patient after patient, ILS classes organize students to revisit the basic science behind a disease and its treatments, to make connections between medical literature and the people in their care.

Penland says she appreciates the perspective her ILS course provides. Brufsky taught her that breast cancer metastasizes into bone. She notes how the woman she just visited complained of hip pain and broke a hip while under treatment for breast cancer.

“I think seeing patients has to be part of the course,” says Penland. “I think it forces students to think outside the box and think about what’s really going on with the patient.”

Explain how he presents topics, she directs students to patient who demonstrate those topics.

Fourth-year students need that kind of clinical correlation, he says. —ET

FOR MORE INFORMATION:
See the Office of Student Affairs site at http://www.dean-med.pitt.edu

Flashback

It seems some details get muddled over time. . . .

“I can’t recollect whether it was a cadaver’s leg or a box of bones I was taking home on the bus to study. The bus came to a sudden stop and whatever it was fell on the floor and slid so that it came partially out of the bag. A lady started to scream. And my response was to rapidly put the items back in the bag and depart the bus—long before my stop.”

—John A. Perri, MD ’59
Appointments

**Thuy Bui** has been appointed director of the Program for Health Care to Underserved Populations and has joined Pitt as an assistant professor of medicine. As director, she oversees the Learn and Serve America Program, sponsored by the Corporation for National Service. In this program, students learn while assisting underprivileged communities, and faculty members serve as mentors and preceptors. She is currently recruiting retired faculty to aid in a senior mentoring student program.

Bui, who formerly worked at the Alma Illery Community Health Center in Homewood, wanted to integrate her desire to teach and reach out to the less fortunate. She was also a Peace Corps volunteer in Malawi, Africa for two years after serving as chief resident at the University of Alabama.

After medical school and a fellowship in Chicago, **Linda Farkas**, a specialist in colon and rectal surgery, has joined Pitt as an assistant professor of surgery.

Farkas, who has published research findings in the area of trauma, is now focusing her attention on fecal incontinence in pregnant women. She plans to conduct a long-term study on that condition and is working to help launch a gastrointestinal clinic at Magee-Womens Hospital. –ST

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**PILE ON THE LAURELS**

Eugene N. Myers, Eye and Ear Foundation Professor and chair of the School of Medicine’s Department of Otolaryngology, has been awarded the Honorary Fellowship of the Royal College of Surgeons of Edinburgh, Scotland. Myers’s research and clinical efforts focus on the treatment of head and neck cancers. His honorary peers at the Royal College, established in 1505, include Mother Teresa and Nelson Mandela. Myers’s Pitt otolaryngology colleague, professor Joseph M. Furman, has been reappointed as chairman of the NASA Peer Review Panel for Neuroscience. The panel reviews neuroscience-related proposals for ground- and flight-based research submitted to NASA’s Life Sciences Division. Furman specializes in managing patients with dizziness and dysequilibrium and directs the otolaryngology department’s Balance Disorders Program.
Musgrave Named Distinguished Alumni Fellow

Ross Musgrave, MD ’43, last performed plastic surgery 10 years ago, but he hasn’t put down the tools of the trade.

Musgrave the artist wields surgical scissors and a scalpel over ribbon and upholstery fabric, skillfully carving it into shapes that he transforms into collages of landscapes and floral still lifes.

His artwork recently earned him a one-man show at a Sarasota gallery. For his nearly 60 years of contributions to the School of Medicine, the University has awarded Musgrave, executive director of the Medical Alumni Association, a 2000 Distinguished Alumni Fellow Award.

“I miss surgery. But I have traded that for close contact with the students,” Musgrave says. Under his 10-year tenure as executive director, the association started a pager rental program for students and instituted a white coat ceremony for incoming freshmen, among other initiatives.

Musgrave’s award acknowledges the remarkable career span of a man who became a doctor at 22. He spent 13 years on the School of Medicine Admissions Committee, six years as a trustee, and 35 years as a clinical professor of surgery. He served as president of the American Society of Plastic and Reconstructive Surgeons and the American Cleft Palate Association. On the side, he mentored students, painted, dabbled in Japanese flower arranging, and performed on stage. “When you do things you like, you find the time,” Musgrave says. That goes for his efforts as alumni association director as well: “I’m having too much fun to stop.” –ET

Just in Time Radiology

IT’S A STORY OF THEFT, BIG MONEY, AND TECHNOLOGICAL INTRIGUE. THE UNEXPECTED CONCLUSION, AS PAUL J. CHANG, ASSOCIATE PROFESSOR OF RADIOLOGY AT THE SCHOOL OF MEDICINE, TELLS IT, IS AN ELECTRONIC SHELL GAME.

We begin with modern medicine’s growing pains. As physicians began sharing patients with multiple specialists in different offices, everyone needed to see the same paper records and X-ray films. And the dirty truth was that physicians often found the best way to get those X-rays was to pilfer them.

Medical records raids became less common with computer technology and Picture Archiving and Communication Systems (PACS), a system for storing and retrieving X-rays electronically. Chang, director of radiology informatics at UPMC, has PACS, a wall of servers wired to a network of $100,000 workstations. Only the largest hospitals can afford PACS, and even Chang’s generous budget is gobbled up by the system. He searched the market fruitlessly for a cheaper solution.

Enter Chang the engineer (he earned an MS in engineering while he was getting his MD from Stanford). A tour of a stereo amplifier factory got him thinking about “just-in-time” manufacturing principles and how they could be applied to radiology. He considered how PACS delivers monstrous amounts of information to a computer, where physicians look at and digest only tiny bits at a time. Chang decided to exploit that mismatch between the large quantity of data radiologists need and the small amount the human brain can handle. His answer was a medical imaging system called Dynamic Transfer Syntax (DTS).

The DTS trick is “streaming” technology. Click on a patient name, and you get the same set of chest X-rays you get with PACS. But with DTS, the information in the images isn’t downloaded until you click on a specific image or section of an image; then any PC can send and receive the high-fidelity details in that section. Not only is DTS less expensive, it’s faster. UPMC has used the system for about a year, and a California company is preparing it for commercial use.

A happy ending, but Chang still is a little frustrated. “I didn’t want to invent this,” he says, “I wanted to buy it.” –ET
To call ginkgo biloba a mere fad would hardly be fair. Ginkgo leaves have been used in traditional Chinese medicine since 1505, according to texts from that era. Strong anecdotal evidence has suggested that something in those leaves may have the power to alleviate depression, cardiovascular disease, macular degeneration, tinnitus, impotence, and a host of other ailments.

And Americans buy it—to the tune of $100 million a year, according to Steven DeKosky, interim chair of neurology and professor of psychiatry, neurology, and neurobiology at the University of Pittsburgh School of Medicine.
No one has applied the rigor of scientific inquiry to reports suggesting that ginkgo can have an impact on the development of dementia. No one, that is, until DeKosky started a study this spring.

“The idea of taking these traditional folk medicines and using modern design to try to confirm the effects they allegedly have is not new,” DeKosky says. “But actually doing the studies is new.”

DeKosky’s $20 million prevention trial is funded by the National Institutes of Health’s National Center for Complementary and Alternative Medicine as well as the National Institute on Aging. The four participating universities—Pitt, Johns Hopkins University, Wake Forest University, and the University of California at Davis—will monitor, over a period of six years, 3,000 initially healthy subjects aged 75 and older living in Pittsburgh, Hagerstown, Maryland, Winston-Salem, North Carolina, and Davis. Half the subjects will be given 240 milligrams of ginkgo daily, the other half a placebo. By way of annual exams that employ neuropsychological testing, MRI, functional measurements, and neurological exams, researchers will monitor how many members of each group develop dementia during the six-year period. A positive diagnosis of dementia is defined by changes in cognitive function scores and changes in functional status. The study will not aim to determine which of ginkgo’s myriad active ingredients—called flavones and ginkgoloids—specifically affect dementia. That’s left to future studies.

Because about 75 percent of the dementias that develop will likely be from Alzheimer’s disease, the study is potentially significant to efforts to prevent that dreaded disorder. DeKosky also is involved in an ongoing 30-city US clinical trial, funded by Switzerland-based Schwabe Pharmaceuticals, on the use of ginkgo to treat Alzheimer’s.

DeKosky points out that aspirin came from tree bark and the heart stimulant digitalis came from foxglove, so there certainly is a history of therapeutic substances prescribed by Western physicians as having such origins. But now, drug companies and academia are taking alternative medicine a little more seriously, investigating what pharmacology might lie behind the folklore.

The prospect intrigues DeKosky: “If you are a physician, it’s hard to watch or listen to all of the claims made by the manufacturers of the nutriceuticals, to see them making claims on the edge of what can be proven, and not want to try to prove some of it.”

WHERE WEST MEETS EAST
The aim of Chinese and Western medicine is essentially the same—to keep the bodily systems in balance. Even the basic diagnostic procedures are similar: observation, palpation, auscultation, percussion, interview. It’s the Eastern treatment modalities that tend to be difficult for the Western mind to wrap itself around. But soon, centuries-old, empirically effective methods of traditional Chinese medicine (TCM) will be put to the test of Western clinical research methods to determine safety, efficacy, and quality. In collaboration with the Chinese Ministry of Science and Technology, the University of Pittsburgh has formed the International TCM Center. The center is supported in part by NIH’s National Center for Complementary and Alternative Medicine.

Though TCM includes a number of different therapies, the center will focus primarily on herbal medicine. It’s a natural tie-in with the drug discovery program at the School of Medicine—and further boosted by the fact that millions of dollars are spent annually by already believing consumers.

—PMP

BEYOND BED REST
A GENETIC LINK TO PREECLAMPSIA
BY SANDY TILNEY

Preclampsia was first described some 2,000 years ago. Yet still, “Get plenty of bed rest” is one of the few pieces of advice physicians are able to give women to help reduce its dangers. Carl Hubel, assistant professor of obstetrics, gynecology, and reproductive sciences, would like them to be able to do more. He along with Robert E. Ferrell, professor of human genetics at the Graduate School of
Public Health, and other researchers at Magee-Womens Hospital believe they are getting closer to understanding the development of this puzzling, sometimes fatal, condition. Preeclampsia, which affects 5 to 7 percent of pregnant women in the United States, results in symptoms such as hypertension, edema (irregular swelling), and kidney malfunction, and is one of the leading causes of fetal as well as maternal mortality.

Hubel’s group has found that a woman’s chances of acquiring the condition are roughly quadrupled if she possesses either of two gene mutations known to result in deficient activity of lipoprotein lipase. When functioning normally, the lipase enzyme maintains appropriate levels of triglycerides.

Caucasian women with preeclampsia show an increased probability of having the mutated gene that produces the dysfunctional enzyme. Hubel elicited these findings by studying three groups of Caucasian women from the Pittsburgh area—a group who experienced normal pregnancies, a group with preeclampsia, and a group of women who weren’t pregnant and were randomly selected without regard to health status. His team is now investigating whether these genotype differences apply to other parts of the world and to other ethnic groups.

Preeclampsia is a polygenetic disorder, which means there is no one gene that contributes to its onset. In addition, environmental as well as lifestyle factors are thought to play a role. So Hubel’s recent findings won’t allow physicians to predict preeclampsia just yet, but they may help the medical community determine the disorder’s mysterious mechanisms.

Gupta and collaborators are using an intact cervical culture for HIV-transmission modeling. They will be among the first to see how the virus is transmitted through the cervix’s diverse and multiple cell layers.

**Gupta Tracks Transmission | By Patricia M. Park**

The exact mechanisms for sexual transmission of HIV are unknown—but for Phalguni Gupta, they are becoming less and less elusive.

Gupta, an associate professor of pathology at the School of Medicine and professor and assistant chair of the Graduate School of Public Health’s Department of Infectious Diseases and Microbiology, is sure that if he can get to the nitty gritty of how HIV is transmitted it will “revolutionize” treatment. Gupta’s wiry frame tenses a bit as he says this. You believe him—there is nothing else that smacks of overstatement in the man.

The medical research community most recently learned of Gupta’s work regarding HIV transmission among men: He discovered that while some viruses are blood-borne, some are actually shed in genital organs, a differentiation he refers to as “compartmentalization.”

His studies showed compartmentalization can affect how quickly the virus is transmitted. More importantly, it looks like what might be an effective treatment for a blood-borne virus cannot be presumed to work for others.

Gupta also has news that he hopes will hold back the growing heterosexual HIV transmission front. His eyes shine with excitement as he explains:

With collaborators from Magee-Womens Hospital, Gupta has developed an organ culture for study of HIV transmission in women. Historically, female transmission models consisted of only single layers of prepared cells; yet the cervix is made up of different kinds of cells in multiple layers. No lab was able to produce a workable model. Not sure how to approach the challenge, Gupta enlisted the help of infectious diseases and microbiology graduate student Kelly Brown, Gregg Naus, associate professor of pathology, and Dan Landers, associate professor of ob/gyn.

The researchers were able to procure and house an intact cervical architecture, obtained through part of a routine surgical repair of an otherwise healthy, premenopausal woman. Gupta’s team applies the virus to the topmost layer of cells and assays it after it has migrated through the remaining cell layers. This opportunity to observe how the virus affects—or is affected by—each layer of tissue could lead to the creation of barrier medications to block the transmission process.

Did somebody say revolution?
At first, nothing changed very much. True, the Pitt medical students who trudged uphill to Pennsylvania Hall, lugging microscopes and copies of Gray’s Anatomy, were now officially members of the US Army or Navy, having raised their right hands short days after the Japanese attack on Pearl Harbor plunged the nation into World War II. But Frank Schwartz,
technically Navy Ensign Schwartz, continued to live in a rooming house on Darragh Street. Bill Donaldson, another ensign, still wore the same old civilian clothes. Ross Musgrave went on waiting tables and operating an elevator nights and weekends, struggling to meet tuition payments that came from his pocket, not Uncle Sam’s.

In 1945, however, after three hurry-up years of Pitt medical education and an internship, Schwartz found himself a battalion surgeon in a field hospital just behind the First Marine Division invasion force on Okinawa. There, he put into practice what he had learned in surgery classes as he nursed a shrapnel wound in his left arm. Donaldson was at Okinawa, too, a ship’s doctor aboard a destroyer escort, dealing with wound treatments and patient evacuation procedures that he had never seen in a medical textbook. Musgrave missed actual hostilities. But just after the Japanese surrender, he was north of Tokyo in a “boony hospital right out of MASH,” setting leg fractures and performing orthopaedic surgery on 11th Airborne Division paratroopers. He was 25 years old and had roughly nine months’ background in orthopaedics.

For those men, now mostly retired from practice, those wartime years in the School of Medicine were signal, seismic-shift events that transformed their lives and their professional careers. Depression-era youngsters who had scrambled for an education, they had hoped for little more than an ordinary Western Pennsylvania practice of flu and fractures, rather than one of emergency amputations, dengue fever, and dysentery.

In the dark days of December 1941, recalls Macy Levine, MD ’43, most Pitt medical students, like millions of other patriotic young men, wanted to sign up to fight. They were dissuaded by the redoubtable Dr. Davenport Hooker, the legendary anatomy professor Levine describes, with a respectful shake of his head, as “a little bit of a guy with a booming voice.

“He told us in no uncertain terms that our duty was to stay in school,” Levine says. “He said we could do a lot more for the country by becoming doctors than by getting killed in the infantry.”

Hooker’s words were being echoed in medical schools across the country. The American Medical Association estimated that 50 percent of the nation’s 140,000 physicians would be needed to treat battlefield casualties, and it was important to keep the pipeline flowing. (In the end, 40 percent of American doctors served, according to Dale Smith, professor of medical history at the Uniformed Services University of the Health Sciences, with many “golden-agers” emerging from retirement to fill civilian needs.)

Medical students were draft-deferred, then quickly sworn in and placed on inactive status until they received their degrees and finished internship. In the years 1942 to ’45, Pitt graduated more than 300 MDs, almost all of whom, with the exception of a few...
women and those with medical deferments, wound up in uniform.

The students, of course, were not the only medical-school personnel who went off to war. Within a year, more than half the teaching faculty was gone, too. “The anatomy and pharmacology faculty was down to four,” Campbell Moses noted afterward. “In normal times, there would have been three times that number.”

Pitt’s medical military contribution actually preceded the war’s outbreak. In 1941, at the behest of the US Surgeon General, Pitt faculty and graduates reconstituted Base Hospital 27, originally set up in World War I. Some 156 medical officers, including 100 nurses, formed the 27th General Hospital, under command of J. R. Watson, a noted Pittsburgh surgeon and faculty member. Among the many Pitt faculty who served in the unit were Major Charles Altman, a urologist, Major John Donaldson, an orthopaedic surgeon, and Captain Leonard Monheim, an anesthesiologist. In July 1944, the unit established a 2,250-bed general hospital in Hollandia, New Guinea, in an area of malarial swamp that had been quickly cleared out of the surrounding jungle. The 27th was the nearest hospital to the island-hopping offensive that would eventually win the Pacific war and admitted 21,054 casualties from battles from Guadalcanal to Luzon. It was the site of the first blood bank in the Pacific theater, and its personnel were many times decorated.

“He said we could do a lot more for the country by becoming doctors than by getting killed in the infantry.”

In fact, Musgrave says, the students were studying harder than they ever had in their lives. The chidings of Hooker and accounts of the war they’d heard made waiting for their turn overseas easier: “It was made clear to us that anyone who flunked out would go right into the military,” Musgrave says. “Knowing that failure made you cannon fodder was the surest form of encouragement to work hard.”

Before the war, the medical school operated on a standard academic calendar—nine months of classes and a three-month summer vacation. In July 1942, at the US Surgeon General’s request, Pitt and other schools switched to a speeded-up “nine/nine/nine” schedule—three nine-month terms with a week off between. Pitt thus graduated three classes of 70 to 80 physicians a year; new students were admitted twice annually. Graduation was followed by a nine-month internship, after which the interns were com-
missioned as first lieutenants (lieutenants, junior grade, in the navy) and assigned to active duty. Thus Musgrave, for example, received his diploma and lieutenant’s bars in December 1943, a full year earlier than the Westminster College grad had expected when he enrolled at Pitt in 1940.

Although medical graduates would be confronted by problems far different from those they might have faced in a civilian practice—from shrapnel wounds and incendiary-bomb burns to malaria and trench foot—the medical school curriculum actually changed very little. As part of a medical ROTC program, the school in 1940 had instituted a course in “military medicine” and made it mandatory for all students of draft age. “Military medicine,” as Musgrave remembers it, consisted mainly of map reading, sanitation, first aid, and combat tactics. Only a few students progressed to an advanced course in military medicine. “We didn’t take military medicine that seriously,” says Al Corcoran, who graduated in 1944. “We concentrated on courses that we considered more important and more difficult, like anatomy, that we absolutely had to master.”

Building on Alexander Fleming’s 1929 discovery, physiologist Howard Florey and his colleagues at Oxford University had further investigated penicillin’s great healing potential in 1940, although it didn’t go into mass production in the United States until 1942. Selman Waksman at Rutgers University had developed streptomycin in 1943. These antibiotics, and sulfonamide, were to play critically important roles in treatment of battlefield and civilian casualties. One medical historian contends that penicillin, not the atomic bomb, was the “secret weapon” that ensured allied victory. But none of these agents were mentioned in class, as nearly as the graduates can recall today. Musgrave’s first experience with penicillin came in 1944. He was an intern at what is now UPMC Presbyterian and called upon to administer injections of the stringently rationed drug every three hours to a VIP for whom a small amount of the precious stuff had been obtained.

It was not until the war was nearly 18 months old that the students were officially mobilized. In May 1943, the military instituted the Army Specialized Training Program (ASTP) and the Navy College Training Program, known as V-12, which sent young men to college to study engineering, dentistry, psychology, foreign languages, and other subjects expected to have military application. More than 500 ASTP privates attended Pitt, living in barracks fashioned on several floors of the Cathedral, marching in formation to classes, and springing to attention when a sometimes-startled civilian professor entered the classroom. The medical students were subsumed into the program, wearing olive drab under their lab coats now that their tuition was paid by Uncle Sam.

As medical students, they were freed from some of the more onerous military requirements. Musgrave and Levine, for instance, were junior interns at the US Marine Hospital (now the Arsenal Medical Center), Donaldson was at Homestead Hospital, and Corcoran was at Ohio Valley Hospital. They slept at the hospitals, receiving room and board but no wages for their duties.

At other times they were subjected to military spit-and-polish. They stood in assembly four afternoons a week; formation and inspection were on Saturday—when they were examined for haircuts (“no hair touching the collar”), clean shaves, pressed uniforms, and shoe shines.

“The constant effort of the men to keep their shoes shined has resulted in the almost complete loss of the fine art of apple polishing,” joked the September 1943 Pitt Anatomy Snooze, a mimeographed bulletin that went to all med-school graduates in the military. Wednesday was given over to “athletics.” “They marched us from the hill to the old Shady Side Academy (where Winchester-Thurston School now stands), or sometimes Panther Hollow in Schenley Park,” Corcoran remembers. “Then we’d have to run around the lake and run back to Pennsylvania Hall. Anyone who fell out had to wash windows.”

Any former student’s reminiscences about wartime classes always seem to come down to Dr. Hooker and his anatomy lab. Students found him both inspiring and intimidating and still speak of him with awe. George Wright, MD ’49, who served as a
battalion surgeon in Korea, continued as a first-year medical student to play in the university band. Hooker called him to his office. “He didn't look up from his desk,” Wright recalls, “just growled, ‘Wright! Do you want to be a doctor or a trombone player?’ I quit the band that day.”

Hooker always lectured from an elevated dais, Donaldson recalls. “Because of his voice and his personality, I thought he must be six feet tall. When I visited the campus after my discharge, I was astounded to find he was only about five feet two.”

The Anatomy Snooze was Hooker’s idea. Issued “now and then,” and consisting of two or three pages, its original purpose was to keep graduates abreast of School of Medicine doings. It quickly turned into a kind of round-robin letter. Far-flung readers updated their classmates on their whereabouts and experiences. Others asked for guidance on medical questions or suggested topics for instruction. Some recommended more student training in psychology, to enable them to identify cases of combat fatigue. Those in the South Pacific asked for slides of intestinal parasites and of malarial or filarial agents. Not surprisingly, some of the correspondence, which was later collected into a book, was given over to gripping. “For a year and a half,” complained one young doctor, who had been assigned to a recruiting station, “my medical career has consisted of saying, ‘Open your mouth. Say, “Ah.” Turn your head so I can examine your ears. Now the other ear. Next.’”

The young men were also handling cases they had never dreamed of back in medical school. Wright, serving in the first grisly days of the Korean War, found himself swamped with cases of balanitis in uncircumcised men who had been unable to shower or undress during six continuous weeks of combat. Schwartz, who was to practice ophthalmology after discharge, was assigned at war’s end to Tientsin, China, where each morning and evening he administered Atabrine for malaria. Correspondents from the Philippines reported treating—or attempting to treat—elephantiasis, schistosomiasis, dengue fever, and leprosy.

Donaldson was in more than 100 air raids. While his destroyer-escort, the USS Barber, was on picket duty off Okinawa, steaming north through heavy Pacific seas, it received a message from a sister ship. A sailor had developed acute appendicitis. The ship’s doctor, a recent young graduate like Donaldson, had never performed an appendectomy, nor even incised the body cavity. The other ship requested that a more experienced doctor be transferred aboard. They wanted Donaldson. At 25, Donaldson had assisted in the operating room as a junior intern and later had “a little training” at the Philadelphia Naval Hospital.

The two ships were roped together so that a breeches buoy could be used as a conveyance. Donaldson was to be seated in the breeches buoy and hauled across the angry waters to the other vessel. First, however, it was decided to send films and texts across the gap. Halfway across, books and films fell into the sea.

“That does it,” the Barber’s captain told Donaldson. “If we can’t get a book across, I’m not going to risk my doctor.” Donaldson stayed aboard the Barber and the other vessel turned back to San Diego.

“I haven’t thought about that in 50 years,” says Donaldson, who has retired from a long career as a surgeon and as medical director of Children’s Hospital of Pittsburgh. Although some memories have faded, alumni agree that the war shaped their lives in important, if subtle, ways. That time, indeed, often determined their post-war residencies or specialties.

“It was amazing, the responsibility given to us so young,” says Musgrave, who at 24 was officially chief of orthopaedic surgery at his 172nd Station Hospital.

“I think the greatest thing about our accelerated education and our service wasn’t what we learned medically,” says Musgrave. “It was the maturation process. That’s what stood us in such good stead when we returned home. And has for more than 50 years.”
Julius Youngner gave polio a run for its money; now he’s tackling the next pandemic.
ne spring morning in 1918, Albert Gitchell didn’t report for duty. Gitchell, an army cook at Camp Funston, Kansas, had a fever, sore throat, muscle aches, and the chills. He was diagnosed with the flu and sent to his quarters for bed rest. By noon that day 107 of his comrades fell ill. Within two days, the number climbed to 522. Victims collapsed with crippling headaches, their skin ranging from blue to purple to black. Bodies piled up three and four deep on morgue floors. The living coughed violently, fought projectile nosebleeds and organ failure, and within three to five days of infection, most drowned as their lungs filled with bloody fluid.

The so-called Spanish flu pandemic swept from continent to continent, leaving a trail more lethal than the world had seen since the sixteenth century. In less than a year, influenza claimed an estimated 30 million lives—about 22 million more than World War I—and vanished as quickly as it arose.

The twentieth century saw three influenza pandemics: After the Spanish flu, the Asian flu of 1957 killed almost 70,000 in the United States alone; the Hong Kong flu of 1968 killed 36,000. Pandemics come in waves, usually one every 20 years, and according to the Centers for Disease Control and Prevention, the United States can expect one to strike at any time, and leave more than 200,000 dead.
Julius Youngner perches on the edge of his reclining office chair, his back to a window overlooking the rainy streets of Pittsburgh. Trim white hair frames a face flush with frustration as he pounds his fists on his desk. Youngner’s voice, which quickly gives away a childhood spent in New York City, is an unusual mixture of soft and smooth with Manhattan wit and edge. Unless he’s speaking about his research.

“I feel very passionate about this,” he says, his voice suddenly thick with New York aggression. “You want to know why passionate? I’ll tell you why passionate. You ever heard of influenza pandemics? 1918? Killed about 30 million? Or Asia? Hong Kong? That’s why passionate.” Then he leans back in his chair and lets out a slow, deep breath through his nose as he folds his arms behind his neck and calms himself.

Youngner, 79, is a distinguished service professor in the School of Medicine’s Department of Molecular Genetics and Biochemistry. He and his colleagues are using a vaccine they’re pretty sure could stop the next influenza pandemic dead in its tracks. Now they’re holding their breath until they can further develop it.

To understand Youngner’s passion, it’s essential to understand three facts about influenza. First, it comes in different forms: influenza A, B, and C. Youngner doesn’t worry himself with B and C, because they’re not the ones tied to pandemics. That’s a job left solely to influenza A.

Second, each flu virus has spiky proteins on its surface which latch onto the cells lining a host’s respiratory tract—this is how the virus infects. These proteins, hemagglutinin (H) and neuraminidase (N), are the way viruses infect a host’s respiratory tract—this is how the virus infects. These proteins, hemagglutinin (H) and neuraminidase (N), are the way viruses get into our bodies.

Third, influenza viruses carry their genetic material on eight segments of single stranded RNA—this means that, instead of having one chromosome with many genes on it, flu has eight little chromosomes, each with genes encoding only 10 gene products. But, because each influenza A strain has a similar eight-segment genome, if two different strains infect the same cell at the same time, they can shuffle genes around, change their HN configurations, and create an influenza strain our bodies have never seen. Sometimes these changes inactivate the virus; sometimes they have no effect at all. But sometimes, they start pandemics and kill millions of people.

Influenza viruses can change through genetic recombination of two known strains or by the introduction of a completely new strain from another species. For example, an influenza strain originating from chickens was found a way to protect against any strain of influenza A—even those not yet in existence.

Dowling and Youngner are studying a human flu vaccine that has already been proven safe and effective; they propose using it as a powerful antiviral.

In the course of his viral research, Youngner found a mutant strain of influenza A that prevents any normal A strain from growing when they’re both in the same cell. He and Dowling called this phenomenon “dominance.” They published papers showing which gene was responsible for dominance, proposed a live influenza vaccine that contained a mutant to inactivate any live influenza A strain it encountered, and landed a grant from NIH for a small safety trial in humans. The results of the trial: no problem.

To probe whether their dominant mutant would be effective against any strain of influenza A, Youngner and his team used cultured cells to test it against every HN combination they could get their hands on—13 in all. In each case, as long as both the dominant virus and the virulent virus were strains of influenza A, the effect was the same: inactivation. According to Youngner, the implications of this finding could be monumental. If a new flu strain came along, this novel vaccine/antiviral—an attenuated live virus acting as a dominant mutant—could be injected after exposure to halt a pandemic before it took off.

“It wouldn’t make any difference if it were H7N7 or anything else. You could stop it,” he

But as he talks, he shakes his head. After Youngner's small trial in humans, his lab's progress has slowed considerably. It seems Youngner and Dowling's work goes against widely held beliefs (which Youngner calls dogma) that a vaccine is only used for prevention, not treatment, and that you don't mix flu viruses because you never know what sort of shuffled virus will come out of the mix. The paralyzing fear: by combining a live virus and a mutant, Youngner may create sort of a "super vaccine," that could lead to a super virus.

Yet he and his colleagues have completed preliminary studies to show that their idea is safe, and that they do know what kind of virus will come out of the mix—an attenuated one. In fact, virologists around the country, even if they aren't entirely sold on the proposed vaccine, say they would like to see Youngner and Dowling take the next step. With so much at stake, that day won't come soon enough for Youngner. The clock is ticking.

Youngner, it seems, is always on the edge or in the middle of the "next big thing." He has witnessed the birth and growth of the field of virology, and with it, more excitement than he could have imagined. It all started with World War II.

With a doctorate and eight weeks of basic training behind him, 23-year-old Private Youngner found himself in a company of 100 men at Camp Barkley, Texas. One day, 99 shipped out. Youngner was the only man left. He asked what was wrong with him, why he couldn't go. No one, not even the sergeant, knew the answer.

For two days Youngner scrounged for meals and slept in an empty barracks, until finally, a jeep drove up. The driver hopped out, said, "Get your stuff," and Youngner soon found himself on a northbound train. His orders—which he couldn't open until he was en route—simply said he was on special assignment, that the military police were not to bother him, and he was to get off at Knoxville, Tennessee, where he should open a second envelope. That envelope contained only a phone number. At 2:00 in the morning, the young private picked up a pay phone in Knoxville and dialed.

"Hello," a voice said flatly.
"Uh, this is Private Youngner. . ."
"Where are you?"
"At the train station."
"Good. There's a bench behind you. Wait, somebody will be there to get you."

So Youngner dragged his barracks bag to the bench, where he used it as a pillow, and quickly fell asleep, only to be awakened by a man hovering over him in a leather jacket.

"You Youngner?"
"Yeah."
"Come with me."
The two men got into a car and drove into the hills.
"Where are we going?" asked Youngner when he couldn't contain it anymore.
"Oak Ridge."
"What's in Oak Ridge?"
"Don't ask any questions."
The next morning, he awoke in a room with about 30 other men, all as confused as he was. Later that day, they were told they were part of the Manhattan Project.

Youngner ended up spending two years in Rochester, New York, studying the effects of uranium salts and determining safe levels of inhalation. Within a few years, he found himself in Pittsburgh, working on another high profile project with the now legendary Jonas Salk.

In 1949, when Youngner arrived in Pittsburgh, Enders, Weller, and Robbins had just proven that polio could grow in cell culture, but Salk and his team were still growing it in monkeys. Youngner knew that until the team grew large quantities of the virus in cell culture, they would never have enough to make a vaccine. He ended up developing trypsinization, a technique for culturing animal cells on a large scale, which exponentially increased the amount of virus they could grow in the lab.

According to Raymond Cypess, president and CEO of the American Type Culture Collection, the largest repository for cell and tissue cultures in the world, trypsinization changed the face of tissue culture investigation.

"Well," says Youngner with characteristic humility, "it was just a technical advance."
Indeed, his technical advance quickly became standard procedure in labs around the country. Once he helped develop the means for producing polio on a large scale, Youngner moved on to inactivate the virus—leaving it crippled enough so it couldn’t cause disease, but active enough to provoke the necessary immune response in patients. He developed tests for quantifying polio and determining its viability; and after six years in the laboratory, the polio vaccine went into what would become a world-famous field trial. Soon, Salk’s voice boomed from television screens and radios around the world, announcing that the vaccine was safe and effective. In the media flurry, Youngner and his colleagues were not publicly acknowledged for their contributions—a point, Youngner will admit, that rankles him. Of course, he’s glad he was able to make the contribution he did. And it’s easy to see that this virologist’s life’s work has not been inspired by headlines. Instead he’s inspired to take on the polios and influenzas that rankles him. Of course, he’s glad he was able to make the contribution he did. And it’s easy to see that this virologist’s life’s work has not been inspired by headlines. Instead he’s inspired to take on the polios and influenzas of the world. What haunts Youngner is the likelihood of another Spanish flu lurking somewhere around the corner; its tauntings are simply too loud for him to ignore.

H e went on to make critical advances in many areas beyond polio: Youngner was the first to demonstrate that nonviral agents could trigger interferon induction, which led to the idea that interferon could have important functions beyond its use as an antiviral. He discovered that some viruses inhibit interferon in cells, which eventually led him to important contributions in the field of persistent viral infections. His advances have helped millions, but they are little known outside a comparatively small circle of peers and contemporaries.

“There are a lot of good scientists in the United States, but Juli goes above that. He’s one of our stars,” says Cypess. “Unfortunately, he’s also one of our most underrated scientists. But he has never sought publicity.”

Youngner chairs the Ethics Committee for the American Society for Microbiology—the biggest biological society in the world, with more than 40,000 members. And in the early ’90s, he was asked to serve on a research integrity adjudication panel at the Department of Health and Human Services. He served on a panel for a scientific misconduct trial—the infamous Baltimore Case, in which Therезa Imanishi-Kari was accused of falsifying research data, and Nobel-prize winning researcher David Baltimore risked his own career to defend his colleague. (After several contentious and visible years of investigation, Imanishi-Kari and Baltimore were exonerated, but not left uncathed.)

“Scientists should be obligated to take part in these things. They can’t just say, ‘No, I don’t want to get involved.’ By definition, because of the work they do, they are involved. And I’m not the kind of person who can ignore that. So, I told my wife, ’I don’t know how long I’m going to be away.’ I went to DC for the trial, and did what I had to do.” He spent two years serving on the panel.

This call to value scientific integrity may well be part of the Youngner genome.

Julius Youngner’s son Stuart is a prominent bioethicist and psychiatry scholar who now heads the Center for Biomedical Ethics at Case Western Reserve School of Medicine in Cleveland.

“There’s a very important lesson I learned from Juli,” says Gail Wertz. “Listen to the data, listen to the facts, and don’t be saddled with preconceptions. Because preconceptions are inhibitory to science, to developing new concepts, to finding out new information.”

“T here’s a very important lesson I learned from Juli,” says Gail Wertz, a former PhD student of Youngner’s and now a professor of microbiology at the University of Alabama. “Listen to the data, listen to the facts, and don’t be saddled with preconceptions. Because preconceptions are inhibitory to science, to developing new concepts, to finding out new information.”

Youngner has been listening to the data for some time now and is ready to make his next move. In his office, looking out at a rain-drenched campus, he rubs his forehead, trying to contain his emotion.

“Today,” he whispers, “there’s nothing for an influenza pandemic. If one hits, there’s nothing we can do except start making a vaccine, and by then it’s too late.”

With Dowling, Youngner has gathered data for years through work in humans, ferrets, and now horses. Their equine vaccine, FluAvert, recently hit the veterinary market with a huge splash. The results coming in from all directions have convinced Youngner and Dowling their vaccine is safe and effective—perhaps even more so than they originally thought. Of course, they are quick to point out, they need to undertake more investigations before it can be licensed for human use.

“The thing about flu is, you never know when a new virus is going to come along,” says Dowling.

“And, like any new approach to science, our idea might not work.

“But it would be so important if it does.”
Even the language is different here. It is perfectly routine to speak of “light bending back on itself” or of its rays being “pumped.” You, an uninitiated visitor, may be warned, “Don’t look directly at the invisible light.”
Careful, you’ve stumbled into the world of Simon Watkins. This small room in the University of Pittsburgh’s Center for Biologic Imaging might not look like much; in fact you might mistake it for a computer storage closet. Yet in the confocal room, “routine” takes on a whole new meaning.

Think: about something 0.2 microns in size—that’s two-tenths of one millionth of a meter. Think: about the idea that photographs of molecules are being taken here. That in much the same way a CT scan shows planes of organs, the center can optically section cells. That here, Watkins is able to capture what happens in functioning tissue in living animals.

Watkins, who directs the center and is an associate professor of cell biology and physiology, is even able to track how cells talk to each other, where communication breaks down, where mishaps occur. And what he finds is often astonishingly beautiful.

You should note though, his dyes and equipment—confocal, electron, and live-cell microscopes—are able to flag components within the very smallest units of life. Even the beginnings of matter. They do not, however, discriminate between good and bad. Rampant cancers are painted as lovely as muscles at rest.

So look closely.
ABOVE:
BLOOMS IN AN UNEARTHLY GARDEN
Or, dendritic cells in culture.
Investigator: Lina Lu
(scanning electromicrograph)

RIGHT:
A COZY FIRE CRACKLING
Or, simian submucosal gland, stained with Lucifer yellow.
Investigator: Robert Bridges
(multiphoton micrograph)
SHOOTING STARS
Or, skeletal muscle fibers.
Blue = nuclei.
Red = dystrophin.
Green = actin.
Investigator: Romesh Draviam
(flourescence micrograph)
You don’t want more than about 30 hours to pass between the time a patient’s cells are removed and the time they’re reinfused into the patient. This keeps Bill Swaney’s schedule tight. Once he has prepared a supernatant, he must work out the finer logistics like negotiating use of the family minivan so that he can rush to and from an investigator’s lab.
Now and then, Bill Swaney gets a call at 3 or 4 a.m. Still mostly asleep, he’ll clumsily lunge for the phone. “Hello?”

Typically it takes several drowsy minutes before he figures out what a dry digital voice is saying on the other end; usually it’s something like this:

“This is 39796. Alert condition one exists.”
“This is 39796. Alert condition one exists.”
“This is 39796. Alert condition one exists.”

“Fortunately,” says Swaney, “it repeats itself about 10 times before you have to reply. That gives you plenty of time to figure out what’s going on.”

Swaney gets these unnerving calls from a small, black monitor sitting on a sterile countertop in an air-locked vault. The machine is hooked up to incubators, deep freezers, and a host of other tools in the Human Gene Therapy Application Laboratory (HGTAL), otherwise known as the clean room.
Swaney has a love/hate relationship with the dial-happy monitor. It can be rude, but it helps him keep one of Pittsburgh’s most promising technologies safe from the outside world. The few windows in the clean room overlook tug boats creeping north on the Monongahela River. Their winding journeys are serenaded by silence, except for a low hum from an industrial air purifier. As the laboratory’s manager, Swaney makes sure the clean room is clean. It’s a 24 hour a day, 365 day a year job. His merchandise is precious.

Swaney oversees production and delivery of human grade viral vectors—the only type fit for use in gene therapy trials. Tucked away in the clean room, you can usually find vectors that have been surgically altered with microscopic scissors in a procedure that modifies their genomes, rendering them unable to reproduce. And hidden within each vector, you can find a therapeutic gene waiting to be delivered into a human cell.

Back in the ‘70s, John Barranger spent untold hours undertaking what would seem to most a peculiar task. On weekends, he combed the streets of Bethesda, Maryland, driving from hospital to hospital, collecting placentas. The MD, PhD was looking to cure Gaucher disease, the most common genetic disorder in the Ashkenazi Jewish population and the most prevalent lipid storage disorder. Gaucher is caused by mutations in the gene coding for glucocerebrosidase (GC), the enzyme that breaks down glucosylceramide, a substance found in all cell membranes. When a normal cell dies, macrophages, white blood cells designed to eat cellular debris, clean up the remnants. In patients with Gaucher disease, macrophages consume the debris, which includes glucosylceramide, but they can’t digest it. Because of this, and the glucosylceramide build-up that follows, Barranger’s patients came to him with deteriorated nervous systems, organs sometimes swollen to five times their normal size, and brittle bones liable to fracture from normal movement. Barranger thought, if he could find a way to supplement their missing GC, he could alleviate their symptoms. Hence the need for placentas. If he was lucky, by nightfall each Sunday, he would have 100 pounds of placenta to bring into the lab Monday morning.

Though he barely got enough for a handful of patients, the GC he derived from placentas worked. Through bimonthly intravenous infusions, GC halted the progression of Gaucher disease, but there was one problem: the cost. From 100 pounds of placenta, Barranger could extract less than 100 milligrams of pure GC. For the dose required to maintain one patient, this translated into $150,000 per year, per patient, for life.

Barranger had developed the sole treatment for Gaucher disease, but he wanted to
find a more reasonable source of GC for his patients. Then he heard about a French laboratory where researchers wielded presses like those once used to squeeze wine from grapes, but theirs extracted clotting factors from placentas. Knowing the material was too precious to discard, the French researchers cultivated a storehouse of leftover placentas. Barranger caught wind of this and thought, Oh, this is what we need. But it didn’t bring down the cost. So he decided to create the enzyme himself.

Barranger isolated and cloned the gene for GC, implanted it in cultured cells and they grew, happily secreting the enzyme in 500-liter cauldrons. But with the price of producing and maintaining cultures, this didn’t lower the cost either.

Since the pathology of Gaucher stems from one cell type that’s produced in the bone marrow, Barranger devised a new plan, one that didn’t depend on production of GC outside the body. He thought that if he transplanted bone marrow from a healthy donor, his patients would produce normal macrophages from the donor’s marrow instead of Gaucher macrophages from their own. He was right. Within 60 to 90 days, his transplanted patients teemed with healthy donor macrophages. But the mortality rate associated with bone marrow transplants, which is about one-third, was much too high. Yet the fact that it worked sent Barranger in a whole new direction: gene therapy.

Barranger came to the University of Pittsburgh 10 years ago and he now holds several titles. He’s director of the HGTAL, professor of human genetics, and associate director of the Pittsburgh Human Gene Therapy Center. And he is only one of dozens of gene therapy researchers at Pitt putting viral vectors into action to find potential cures for genetic disorders.

The path Barranger took to gene therapy is one shared by many investigators seeking cures for the 5,000 or 6,000 disorders which, like Gaucher disease, result from mutations in single genes. As they learned more about genetics, researchers began to think, Why not replace the abnormal gene with a normally functioning one? It seemed this approach would produce therapeutic results with fewer complications. They were on to something. The field took off.

“Pittsburgh is poised to become a world tertiary medical center for gene therapy, much like it is in transplantation.”

“We have centers in muscular dystrophy, juvenile diabetes, and cardiovascular disease,” he says.

“We are deep into research on gene therapy for neurologic disorders, cancer, metabolic diseases, arthritis . . . Few institutions have even come close to that kind of breadth.”

Pitt researchers have identified a gene that treats muscular dystrophy in animals and one that is important for stopping the blockage of blood vessels. Some Pitt labs are genetically manipulating stem cells to treat muscular diseases. Others are developing genetic therapeutics for pain, sudden heart failure, hemophilia, cystic fibrosis, and other disorders. Much of the work at Pitt has landed in clinical trials—including the first-ever trial for arthritis gene therapy. And this year, trials begin for treating brain cancer and muscular dystrophy.

“As the technology improves,” says Glorioso, “Pittsburgh is poised to become a world tertiary medical center for gene therapy, much like it is in transplantation.”

But how to go about improving the technology isn’t as clear-cut as some might wish. According to many Pitt researchers, gene therapy offers the most promising treatment
Options for thousands of genetic disorders, but it's a road not yet traveled. And recently, the route has proven itself full of potholes and detours that lie as deep in politics as they do in science.

According to its critics, the problems with gene therapy are that it can't be withdrawn once it's instituted, the long term effects aren't entirely known, and researchers are forging ahead without knowing exactly what's in front of them. But, according to its proponents, this is an old tale that's illustrative of the history of clinical trials.

In the eyes of many at Pitt, there is little difference between gene therapy and, say, organ transplantation. Both represent extreme long-term solutions to chronic conditions. According to gene therapists, the big difference, at this point, is that organ transplantation is accepted, gene therapy is not. But things used to be different. The field of gene therapy progressed rapidly until last September, when Jesse Gelsinger, a young man enrolled in a gene therapy study at the University of Pennsylvania, died mid-trial. At this point, no one is clear on the exact role gene therapy played in his death, though it has been implicated, or whether there were mistakes on the part of researchers or regulators. What they do know for sure is that Gelsinger's death brought media focus, public fear, and the field of gene therapy directly into the spotlight.

"The truth is," says Michael Gorin, interim chair of the Department of Human Genetics, "any chronic therapy probably has some risks that we can't perceive in the short term, so we have to be careful and we have to go slowly. But we can't expect this to be complication free. Look at how many deaths occurred in the early days of organ transplantation. Look at how many people still die from organ rejection and the complications of the drugs. We know that, we understand that, and we factor it into our thinking about gene therapy, but we can't let it be an end to the field."

"There are going to be risks," he says, "and people need to be informed, but they have the right to assume those risks." As of yet, no one knows for sure how big those risks might be. During the last decade, about 6,000 patients underwent gene therapy treatments; Gelsinger's death was the first verifiably linked to the trials.

According to Glorioso, the problems facing gene therapy are growing pains in the field. "But to put a positive spin on it," he says, "there are children right now who have been cured of an immunodeficiency syndrome, other patients are being treated for a clotting disorder, and those results look promising too. So, I think we're starting to see the field turn a little bit. Within a decade, we will see lots of these problems resolve."

Growing pains or not, skeptics abound in gene therapy.

In a recent issue of Science, Leon E. Rosenberg, former president of the American Society of Human Genetics, pleaded with gene therapists to "heal thyself." He argues that seeking progress is well and good, but that gene therapists should hold back on publicity until they have unequivocal evidence behind their claims. But for those whose hearts and minds are in the midst of gene therapy advances, it's hard not to be excited by what they're seeing. Progress with Gaucher disease is a case in point.

Barranger's work in gene therapy has really only just begun. After cloning the GC gene and using it to grow the enzyme in culture, he developed a retroviral vector to carry the gene into patients' cells. He used a mouse retrovirus which has never been linked to disease or untoward effects in humans. But to add another safety cushion, Barranger delivered his vectors ex vivo. This means that, unlike direct vector injection into the blood stream—the highly controversial method used on Gelsinger—the viruses

**Vectors are, without question, heavily regulated organisms. The slew of procedures each must undergo just to obtain certification requires, at a minimum...**

**a seven-volume text and $75,000 to $100,000.**
never actually enter a patient's body.

In ex vivo delivery, the method utilized by all Pitt gene therapy trials to date, the cells targeted for gene delivery are carefully removed from the patient's body. Immediately following removal, they're given to a laboratory technician who carries out a list of procedures to remove any untargeted cells. Then the researchers look for Bill Swaney's phone number.

There's a large common area in the clean room, complete with a certified blood bank refrigerator and a sink that produces pure injection-grade water. Swaney calls this "the kitchen." After an investigator, such as Barranger, has obtained approval from the University's Institutional Review Board, the Food and Drug Administration, the Institutional Biosafety Committee, and the Recombinant DNA Advisory Committee (which reports directly to the National Institutes of Health), Swaney prepares for the next steps. He spends three weeks cleaning the clean room before bringing the vector into the kitchen, where he carefully turns it into, what he calls, "soup." On an average day, Swaney and his colleagues make about 10 liters of soup, a.k.a. the supernatant, or liquid substrate containing massive quantities of human-grade vector.

When the investigator's sample is pure, he or she calls Swaney. This time he is wide awake and waiting for the call. After he hangs up, he jumps into his car, drives to the investigator's lab, picks up the cells, and rushes back to the clean room.

There, Swaney mixes the cells with his special soup, where they sit for four hours. He then collects samples, runs final tests, hops back into his car, and rushes back to the investigator, who draws the cells into a syringe and returns them to the patient within 30 hours of their removal. The patient's body never actually sees a virus.

"We're pretty confident," says Barranger, "after almost 10 years of research, that retroviruses handled in this way are safe. They aren't safe if you don't handle them properly; but if they're handled in a replication defective way and ex vivo, there has never been a side effect."

Vectors are, without question, heavily regulated organisms.

The slew of procedures each must undergo just to obtain certification requires, at minimum, compliance with the rules and regulations promulgated by a seven-volume text and $75,000 to $100,000. And that says nothing of production costs. But there's good reason for this extensive caution. These vectors will infect human cells, integrating their DNA into that of the patient's, where it will stay for life. There is no room for error. This is why Swaney covers himself head-to-toe in bio-protective clothing and scours the clean room daily for abnormalities. He's not just running a lab, he's helping to protect future patients from harm.

As part of running the clean room, Barranger and Swaney help investigators keep on top of things. They stay in contact with the FDA to assist Pitt laboratories in maintaining federal standards; they provide guidance for researchers on meeting RAC and IRB requirements; and once a project evolves into a clinical trial, they can also advise and assist along the way.

Of course, when all goes well, the vectors from the clean room never cause disease. Rather, they deliver genes with the potential for curing disease. So far, the University's track record is perfect.

The results of Barranger's clinical trials are keeping his gene therapy wheels spinning; he's now considering ways of refining his technique. Of the four Gaucher patients he treated, one has shown clinical improvement.

"That individual was withdrawn from enzyme therapy without a clinical decline," says Barranger.

The therapy was effective for about three years, but now the repaired cells have begun disappearing. So Barranger is deciding whether to put the patient on enzyme therapy, in spite of its cost, or to try transplanting more corrected cells.

"It's a fundamentally safe approach," says Barranger, of the gene therapy.

"And now we are looking at ways to put the gene into more bone marrow cells so they engraft well into the person from whom they were removed."

Through gene therapy, Barranger thinks he has finally found a way to bring down the cost of treating Gaucher. And because he finds the potential of the treatment so enticing, he hopes he is doing his part to fill in some of the potholes on gene therapy's bumpy road, smoothing the way for future research.

FOR MORE INFORMATION:
http://www.pitt.edu/~rsup/phgt/

GENE THERAPY 102

If or when gene therapy research moves into the germ-line arena, researchers will face a big question: How far do you go? Should parents be able to engineer their offspring, to give their children traits they wish they had? "It's going to be a challenging question," says Michael Gorin, interim chair of the Department of Human Genetics. "It's a natural right of people to want to provide their children with the best advantages and opportunities possible."

Society, he points out, will have to decide which traits are acceptable to alter and which are not. Diseases like Li-Fraumeni syndrome, which causes people to suffer from a list of cancers so long no one's sure what's on it, may fall into the "acceptable" category. It is a fair bet that traits like shoe size and eye color will fall under "unacceptable," but no one really knows. —RS
One more white-coated faculty member files in and the remaining seats are filled. The conference room table stretches long enough for two end-on-end games of shuffleboard. Of course, there are no games here. Instead, Edward Curtiss announces a quorum is present and calls the meeting to order, just as he has every Wednesday this spring. In the next hour or two, this assemblage will decide careers, careers of people who aren’t even at this table. The business at hand: the fate of a few dozen hopefuls who have applied to the University of Pittsburgh School of Medicine. Will these would-be doctors join the ranks of the few hundred this admissions committee admits, or will they be counted among the several thousand who are either rejected or deferred to the wait list?

Methodically, Curtiss, who is the associate dean for admissions and the committee chair, begins reading down a list of applicants. The others keep pace leafing through stacks of paper in front of them. It isn’t long before a voice raises in response to a name.

“Why did we interview this one so late?”

Curtiss, who seems to possess an encyclopedic memory, reports the dates when she applied and interviewed.

“So is she really interested in us?” another asks.

“She has been all over the place,” responds the chair. “This is a lady who is committed to the curriculum we have and the kind of school we have. Her significant other is going to [a faraway school], but
she is interested here. She's very confident and outgoing—a terrific woman who would do well in PBL [problem-based learning].” With this endorsement, questions recede and Curtiss goes back to the group.

A few names later, another member offers an assessment of an applicant.

“In my interview with him, he was a bit overwhelming. It seems he was trying to be funny, but he wasn’t.”

This triggers some critical exchange.

“Maybe he was just nervous. Yes, probably, but . . . . He doesn’t seem to have any clinical exposure. . . . Seems he doesn’t really know himself or what he wants.”

It’s obvious that the prospect is not gaining the committee’s collective favor.

“Was he accepted by [another school], and I don’t think we should deprive our sister school of this candidate.”

After a few chuckles, the committee members probe deeper: they’re not about to act rashly in this business. They surmise that the candidate’s awkwardness belies a lack of self awareness and suspect he is not quite mature enough to contribute fully to the program here. Finally, a motion is made to reject. This is a fairly rare event for the committee. Only a quarter of the applicants even make it this far.

“At least he won’t know he was rejected by committee,” Curtiss says.

Mark Tsai, MD ’01, has sat in on many of these meetings. He recalls how intimidated he was his first time here. Like the accomplished physicians and researchers around him, he was asked to evaluate applicants. But who was he, then a second-year med student, to tell his instructors which applicants were worthy?

“It didn’t take long for Tsai to summon the wherewithal to offer his opinion; and to his surprise, the group was interested in what he had to say. They encouraged him, in fact. Of course, it was explicitly because of Tsai’s perspective as a student that he and five of his peers were appointed to the make-or-break panel.

“One of the original goals when we established the new curriculum [in 1992] was to regard students as colleagues,” Curtiss says. Like their faculty counterparts, students on the admissions committee are required to screen a share of the applications the school receives and make recommendations to the group. Two committee members grade each application, and only those receiving two B+s or better are granted interviews (a B average’s chance for an interview is up to committee vote). A student can be an applicant’s strongest advocate or harshest critic, notes Tsai, who screened 139 applications this year amid the rigors of third year rotations.

“In some ways, we might relate more closely to what a person our age does than someone who is 30 or 40 years older. We tend to have a slightly better understanding of what activities or values are important to applicants.”

Naturally, portions of the admissions process are formulaic. For instance, the gatekeepers aim to preserve an average MCAT score of 10.5 and undergraduate science GPA of 3.66. Of the something like 4,600 applications the school received this year, more than half were rejected because they were either incomplete or did not meet the requisite criteria.

Eventually there’s less science and more sense. “We narrow down the list based on who we think will contribute to our school’s problem-based learning environment and the profession,” says Curtiss. The school offered about 1,100 prospects interviews and 950 showed up. From those, about 500 were put on the wait list. Fewer than 100 were rejected at that point—including the young man who came across as a little immature for the program in the committee’s estimation.

If your name is spoken around Curtiss’s table in March, it probably will boil down to what you are made of. Character is a heavy deciding factor. The school aims for 150 new students who have the initiative, energy, and creativity to excel as clinicians and maybe even as professors and researchers. Intelligence is important, Curtiss says, “but we’re not looking for nerds or wallflowers. To succeed here and as a doctor, you need to be a well-rounded person. . . .”

“For Tsai, a high-ranking graduate of UCLA who interviewed at 10 other medical schools, this access helped close the deal.

“The people you spend medical school with determine what kind of physician you’ll become,” he says.

So it makes sense to Tsai that he was asked to serve on the admissions committee. Students have a right to hold certain expectations of their colleagues, expectations that mirror the school’s standards and values.

“We don’t necessarily expect you to get the highest scores,” says Tsai, “but we do expect you to be committed to medicine, to work well with other people, to experience life, and to know who you are.”

“We aren’t looking for nerds or wallflowers.

To succeed here and as a doctor, you need to be a well-rounded person. . . .”

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The school pays close attention to what challenges or life-building experiences you have faced along the way. You might be a Harvard biology major with a 3.8 GPA and an interest in research, but that’s not necessarily enough. The committee may be more likely to lean toward that sharp kid from a state university, who wasn’t Phi Beta Kappa, but is the first in his family to attend college and also volunteered at the local soup kitchen and helped out in his professor’s lab.

In May, the tables start to turn a bit on Curtiss, Tsai, and the other committee members. In the end, the best of the best must pick them—or Pitt anyway—over what is likely to be some stiff competition. And a lackluster financial aid package is one hardship Curtiss and his committee have traditionally dealt with when making offers. Peer institutions tend to have endowments that are significantly larger, though Pitt has made it a priority to increase its scholarship funds.

The school ends up promoting its challenging yet congenial environment—or “ambiance,” as Curtiss puts it—in addition
<table>
<thead>
<tr>
<th>MATCH RESULTS</th>
<th>CLASS OF 2000</th>
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**ANESTHESIOLOGY**
- Aieder, Miriam  
- University Health Center of Pittsburgh, PA
- Bimbau, Paul  
- University Health Center of Pittsburgh, PA
- Blodgett, Todd  
- University Health Center of Pittsburgh, PA
- Kamenski, Robert  
- University Health Center of Pittsburgh, PA
- Penland, Shannon  
- University Health Center of Pittsburgh, PA
- Ray, Barry  
- University Health Center of Pittsburgh, PA
- Reid, Carl  
- University Health Center of Pittsburgh, PA
- Sarge, Todd  
- Beth Israel Deaconess Medical Center, MA
- Wilson, Shaya  
- The Mount Sinai Hospital, NY

**DERMATOLOGY**
- Rohrer, Carol  
- University Health Center of Pittsburgh, PA
- Ziras, Matthew  
- University Health Center of Pittsburgh, PA

**EMERGENCY MEDICINE**
- Buxko, Jonathan  
- Albany Medical Center Hospital, NY
- DeCaprio, Michael  
- Christiana Care Medical Center of Delaware, DE
- Doshi, Ankur  
- University Health Center of Pittsburgh, PA
- Hernandez, Manual  
- Temple University Hospital, PA
- Kurtek, Richard  
- Maricopa Medical Center, AZ
- McCoy, Matthew  
- University Health Center of Pittsburgh, PA
- Pellegrino, Christopher  
- Penn State Geisinger Health System, PA
- Stutz, Stanley  
- Albany Medical Center Hospital, NY
- Whited, John  
- University Health Center of Pittsburgh, PA

**FAMILY PRACTICE**
- Baghi, Anoushka  
- UPMC St. Margaret, PA
- Cramer, Nancy  
- The Washington Hospital, PA
- Emeron, Jon  
- St. Joseph's Hospital Health Center, Syracuse, NY
- Friedlander, Mary Pat  
- UPMC St. Margaret, PA
- Goldberg, Deborah  
- Abington Memorial Hospital, PA
- Jesteaud, Gregory  
- University of Virginia, VA
- Johnson, Libby  
- St. Mary's Health Services, CA
- Johnston, Pauline  
- Strong Memorial Hospital, University of Rochester, NY
- Jordan, Becky  
- UPMC St. Margaret, PA
- Klein, Amanda  
- Greater Lawrence Family Health, MA
- Mathers, Lawrence  
- Medical College of Wisconsin, WI
- Matties, Carol  
- George Washington University Hospital, DC
- McIlhenny, Angela  
- Allegany Family Physicians, PA
- Oser, Sean  
- UPMC Shadyside, PA
- Oser, Tamara  
- UPMC Shadyside, PA
- Perry, Adam  
- Christiana Care Medical Center of Delaware, DE
- Scheck, Tara  
- UPMC Shadyside, PA
- Suderman, Jeffrey  
- UPMC St. Margaret, PA
- Wasington, Amy  
- UPMC St. Margaret, PA

**INTERNAL MEDICINE**
- Bump, Gregory  
- University of Michigan Hospitals, MI
- Daskalakis, Nikk  
- Southwestern Medical School  
  University of Texas, TX
- Derrah, Robert  
- Internal Medicine Residency  
  Brown University, RI
- Desai, Sachin  
- Rush - Presbyterian - St. Luke's, IL
- Gray, Nicolas  
- University Health Center of Pittsburgh, PA
- Greeno, Neath  
- William Halford Medical Center, Lackland AFB, TX
- Han, Tint  
- Rush - Presbyterian - St. Luke's, IL
- Hutchinson, Patricia  
- Madigan Army Medical Center, WA
- Joseph, Raymond  
- University Health Center of Pittsburgh, PA
- Kates, Steven  
- University Health Center of Pittsburgh, PA
- Malde, Rajiv  
- McGraw Medical Center  
  Northwestern University, IL
- Malik, Aarti  
- McGraw Medical Center  
  Northwestern University, IL
- McClure, Amy  
- Kaiser Permanente - Los Angeles, CA
- Melo, Robert  
- Penn State Geisinger Health System, PA
- Mohat, Prasoa  
- Genesee County Medical Center, MI
- Myrberg, Michael  
- University Health Center of Pittsburgh, PA
- Perkins, Robert  
- Madigan Army Medical Center, WA
- Rice, Robert  
- University Hospitals of Cleveland, OH
- Richards, Thomas  
- Brooke Army Medical Center, TX
- Spaling, Kevin  
- McGraw Medical Center  
  Northwestern University, IL
- Tadakishi, Edward  
- University Health Center of Pittsburgh, PA
- Thai, Dang  
- St. Mary's Medical Center, CA
- Yeager, H. Clay  
- Scripps Mercy Hospital, CA
- Zaleski, Diane  
- University Health Center of Pittsburgh, PA

**INTERNAL MEDICINE PRIMARY**
- Amorid, David  
- Fletcher Allen Health Care  
  University of Vermont, VT
- Nays, Alice  
- Oregon Health Science University, OR
- Nays, Navin  
- Oregon Health Science University, OR
- Nelson, Cynthia  
- University Health Center of Pittsburgh, PA
- Oehlers, Stephen  
- Yale - New Haven Hospital, CT
- Saccio, David  
- Medical College of Virginia, VA

**INTERNAL MEDICINE PEDIATRICS**
- Akara, Rebecca  
- Hospitals of Cleveland, OH
- Anton, Lee  
- Jackson Memorial Hospital, FL
- Ayala, Jose  
- Beaumont Hospital, MI
- Caciody, Renee  
- University of North Carolina Hospital, NC
- Gonzaga, Alda Maria  
- University Health Center of Pittsburgh, PA

**MAXILLOFACIAL SURGERY**
- Reda, Rik  
- University Health Center of Pittsburgh, PA
- Sweeney, Brian  
- University Health Center of Pittsburgh, PA

**NEUROLOGY**
- Berman, Sarah  
- Johns Hopkins University, MD

**OBSTETRICS GYNECOLOGY**
- Both, Karen  
- Thomas Jefferson University, PA
- Harkness, David  
- The Ohio State University Medical Center, OH
- Jackson, Jennifer  
- McGraw Medical Center  
  Northwestern University, IL
- McLaughlin, Beth  
- Brigham & Women's Hospital, MA
- Rice, Cherie  
- The Ohio State University Medical Center, OH

**OPHTHALMOLOGY**
- Erfanger, Michael  
- Nassau County Medical Center, NY
- Im, Lily  
- University Health Center of Pittsburgh, PA
- Keverle, Andrew  
- University Health Center of Pittsburgh, PA
- Vanta, Daniel  
- University of California - Davis, CA
- Murn, Rickard  
- University of Missouri - Columbia, MO
- Marcovitch, Adam  
- University of Michigan Medical Center, MI

**ORTHOPAEDICS**
- Essay, Jon-Eric  
- University Health Center of Pittsburgh, PA
- Johnson, Bryce  
- McGraw Medical Center  
  Northwestern University, IL
- Lowenstein, Jason  
- New York Presbyterian Hospital - Columbia, NY
- Phaffle, Hugo James  
- University Health Center of Pittsburgh, PA

**OTOARYNGOLOGY**
- O'Brien, Erin  
- University of Iowa Hospitals & Clinics, IA

**PATHOLOGY**
- Lai, Keane  
- University of Washington Affiliated Hospitals, WA
- Schneegost, John  
- University of Virginia, VA

**PEDIATRICS**
- Burget, Michelle  
- Medical College of Virginia, VA
- Clayton, Michelle  
- Virginia Medical School, VA
- Derou, Alison  
- University Health Center of Pittsburgh/  
  Children's Hospital of Pittsburgh, PA
- Friedlander, Eric  
- University Health Center of Pittsburgh/  
  Children's Hospital of Pittsburgh, PA
- Goude, Brett  
- Rhode Island Hospital  
  Brown University, RI
- Goyal, Anu  
- Children's Hospital of Philadelphia, PA
- Misra, Kiran  
- Children's Hospital of Philadelphia, PA
- Newton, Kimberly  
- New York Presbyterian Hospital  
  Cornell, NY

**PLASTIC SURGERY**
- O'Brien, Sarah  
- University Health Center of Pittsburgh/  
  Children's Hospital of Pittsburgh, PA
- O'Neill, Christine  
- University Health Center of Pittsburgh/  
  Children's Hospital of Pittsburgh, PA
- Ouellet, Jennifer  
- University Health Center of Pittsburgh/  
  Children's Hospital of Pittsburgh, PA
- Tuite, Vivian  
- University of Maryland Medical Center, MD

**PEDIATRICS EMERGENCY MEDICINE**
- Visocci, Chad  
- Indiana University School of Medicine, IN

**PEDIATRICS PRIMARY**
- Alpert, Navin  
- The Mount Sinai Hospital, NY
- Reitz, Suzanne  
- University Health Center of Pittsburgh/  
  Children's Hospital of Pittsburgh, PA

**PHYSICAL MEDICINE AND REHABILITATION**
- Tsiang, Spencer  
- New York University Medical Center, NY

**PLASTIC SURGERY**
- Kim, James  
- University of California Davis Medical Center, SACRAMENTO, CA

**PSYCHIATRY**
- Aremila, Pamela  
- University of New Mexico, NM
- Berman, Robert  
- New York Presbyterian Hospital - Columbia, NY
- Catapano, Edgar  
- University Health Center of Pittsburgh, PA
- Schlesinger, Abigail  
- University of Michigan Hospitals, MI

**RADIOLOGY DIAGNOSTIC**
- Alarcon, Romina  
- University Health Center of Pittsburgh, PA
- Bierhaus, Andrew  
- Barnes - Jewish Hospital, MD
- Brown, Michael  
- Medical University of South Carolina, SC
- Cantwell, Michael  
- University of Chicago Hospitals, IL
- Hughes, Marion  
- University of Michigan Hospitals, MI

**RADIATION ONCOLOGY**
- Graft, Stephanie  
- New England Medical Center, MA

**RESEARCH**
- Hilsa, Sh Abbas  
- Research in Dermatology

**GENERAL SURGERY**
- Dharmarajan, Seetha  
- Barnes - Jewish Hospital, MD
- Jaffers, Daniel  
- Guthrie/Robert Parker Hospital, PA
- Maung, Adrian  
- Massachusetts General Hospital, MA
- Mollica, Collene  
- Barnes - Jewish Hospital, MD
- Morara, Robert  
- Virginia Mason Hospital, WA
- Neuman, Heather  
- University of North Carolina Hospital, NC
- Pratt, Hugh  
- Tulane University School of Medicine, LA
- Watson, Gregory  
- University Health Center of Pittsburgh, PA

**UROLOGY**
- Fathman, Nicole  
- University of Virginia School of Medicine, VA
- Huang, George  
- New York University Medical Center, NY
- Shapiro, Andrew  
- University of Texas Medical School  
  Houston, TX
By Thomas Mitchell

S
oon researchers will be walking through the inner ear, past the snail-shaped cochlea, and on through the auditory nerve. Unlike the characters in Isaac Asimov's *Fantastic Voyage*, they won't shrink to microscopic size and slip into people's bodies. They'll be using virtual environments and other tools at the new Medical Virtual Reality Center (MVRC) at the Eye and Ear Institute in order to understand better the connections between the inner ear, vision, and balance.

Some pretty fantastic stuff will happen at the new facility and it won't be sci fi, promises Joseph Furman. Furman is a neurologist by training and—believe it or not—a professor of otolaryngology, bioengineering, physical therapy, and neurology. He's working with Mark Redfern, an associate professor with appointments in otolaryngology and bioengineering, and has enlisted the help of colleagues in a number of disciplines to design the MVRC. It will advance both basic research as well as programs for diagnosing and treating balance disorders. The creation of the center is supported by recent and generous grants from the Eye and Ear Foundation.

Almost all of the MVRC projects deal with the link between vision and balance, and Furman expects the new center will see a great number of people with balance disorders caused by aging or anxiety.

One of the most common balance disorders is associated with fear of heights. And, well, "you can't just take someone to the edge of a cliff and let them practice," Furman says. But he can take them to the MVRC, where they might enter a room lined with screens, get strapped into a protective harness, and suddenly find themselves in a virtual glass elevator "travelling" up and down. Such simulations will help investigators learn more about the influence of vision on balance and treating patients using balance rehabilitation therapy. The best part: Nobody has to go to the edge of a cliff.

By Paul Pegher

During his undergraduate years at Pitt in the mid 1930s, Paul Rike took a few electives like tap dance and golf. One afternoon out on the links, the instructor pointed in the direction of a well-dressed foursome. "See those doctors over there?" he asked. "You want to make money and have time to golf? Medicine's what you go into." Rike, who was considering teaching biology for a living, decided to give it a shot.

He never stepped foot on a golf course again—or tap danced for that matter.

Instead, through 50 years of active practice, he earned a citywide reputation for his work ethic. Whether practicing internal medicine at Magee Hospital (as it was then called), consulting at Western Psychiatric Institute and Clinic (where he was the original cardiology consultant), or guiding students as a clinical assistant professor at Pitt, Rike roamed Oakland's halls of medicine, nearly all hours of the day, seven days a week. Former colleagues marveled at his professional decisiveness, accuracy, and the ease with which he would conduct a physical and churn out a hand-written, two-page history. "He is a physician's physician," says David Katz Jr., an obstetrician/gynecologist at Magee-Womens Hospital.

Rike explains his dedication in simple terms. "You're a doctor—that's what you do. But you like it!" he says with a tone of modesty befitting a man who, along with his wife, Hazel Rike, has resided in the same Fifth Avenue apartment for nearly 45 years.

In the vein of lifelong commitment, the Rikes have established a charitable trust worth $1.5 million for the Paul M. Rike, MD, and Hazel M. Rike Medical Scholarship. The Rikes created the scholarship to help attract high-caliber medical students, with preference to applicants from Pennsylvania. Beginning this fall the trust will offer five students $15,000 each a year, over the course of four years, to defray tuition costs.

The Rike scholarship is a big step forward for the School of Medicine. It will help the school bring its financial aid package to the level enjoyed by its peers, many of whom are private and well funded.

"Everyone knows Pitt has one of the best medical schools around," Rike explains. "Students who apply here also apply to Johns Hopkins, Columbia, or Harvard. If they get accepted by three different schools, they will go where they can get a grant; so Pitt ends up losing a lot of good students."

As an instructor, Rike required his students to know everything he did, maybe more. Once a week, he would quiz them on *Cecil's Textbook of Medicine*. More importantly, he strove to instill in them the highest level of respect for their patients and profession. Perhaps it's no coincidence, then, that the preface to *Cecil's* 20th edition states, "Becoming a physician has meaning far beyond completing medical school and residency. It is the entry to a way of life. There are no part-time professionals."

By Paul Pegher

Better than Par

The Rikes donate $1.5 million

Hazel and Paul Rike

Fantastic Voyages

VR Center funded

-by Thomas Mitchell

98.6 Degrees

People and programs
that keep the school
healthy and vibrant

The Rikes donate
$1.5 million

By Paul Pegher

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CLASS NOTES

’40s  JAMES F. CULLETON, MD ’43, attributes his early interest—and 50 year career—in neurophysiology and teaching to his early association with Davenport Hooker. Retired now, Culleton received an AMA Certificate of Merit in 1993.

’50s  JOHN OSTERRITTER, MD ’50, retired locally after a long academic and professional career in chemical/industrial medicine. He received his master’s in public health in 1952 and his PhD in 1955.

’60s  SHELDON WEINSTEIN, MD ’63, is president of the Society of Gynecologic Surgeons and a clinical professor at the Presbyterian Hospital of Dallas, Texas.
ROBERT D’AMBROSIA, MD ’64, professor and chair of the Louisiana State University Department of Orthopaedic Surgery, has been elected president of the American Academy of Orthopaedic Surgeons.

JOHN KRAUS, MD ’66, is chair of the Department of Pathology and Laboratory Medicine at Tulane University Medical Center in New Orleans.

’70s  AARON M. LEVINE, MD ’71, was recently named Physician of the Year at the Memorial Herman Hospital in Houston, Texas. He is president of the PM&R Society there.

TIMOTHY EBERLEIN, MD ’77, is Bixby Professor and chair of the Department of Surgery at Washington University School of Medicine in St. Louis. He was recently elected treasurer of the Society of Surgical Oncology. Eberlein also serves as surgeon-in-chief and director of the Siteman Cancer Center at Barnes-Jewish Hospital.

NANCY STORY SOMERS, MD ’78, received the Distinguished Service Award from Geneva College in Beaver Falls, Pennsylvania, her undergraduate alma mater. She is medical director of Sycamore Manor Health Center and an employee health physician for Liberty Mutual Insurance Company.

’80s  MARK K. LYONS, MD ’86, is an assistant professor and chair of neurological surgery at Mayo Clinic in Scottsdale, Arizona.
NICHOLAS A. KING, MD ’89, was inducted into the American Academy of Orthopaedic Surgeons at the Academy’s 67th annual meeting in March.

AARON M. LEVINE, MD ’71, was recently named Physician of the Year at the Memorial Herman Hospital in Houston, Texas. He is president of the PM&R Society there.

’90s  LISA INOUYE, MD ’90, directs the Internal Medicine Residency Program at Portsmouth Naval Medical Center in Portsmouth, Virginia. A fellow of the American College of Physicians and American Society of Internal Medicine, Inouye is an assistant professor of medicine at both the Uniformed Services University of the Health Sciences and the Eastern Virginia Medical School.

SCOTT ELTON, MD ’94, finished his stint as chief resident in neurosurgery at Ohio State and started a fellowship in pediatric neurosurgery at the University of Alabama-Birmingham. He can be contacted at scott_elton@hotmail.com

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REUNIONS

BACK IN TIME

More than 100 docs and their guests foxtrotted in the Pittsburgh Athletic Association’s (PAA) ballroom with the Jack Purcell Orchestra on May 19 at the School of Medicine’s Annual Alumni Dinner Dance.

But folks stopped dancing long enough for Chancellor Mark A. Nordenberg and Robert Lee, MD ’56, to open a 90-year-old time capsule that had been placed in the cornerstone of the now demolished Pennsylvania Hall (former home to the School of Medicine). Its contents included these must reads—“Instructions and Regulations of a Competition for the Selection of an Architect and the Procuring of a General Architectural Plan for the Western University of Pennsylvania in the City of Pittsburgh, Pennsylvania” as well as the “University of Pittsburgh Bulletin Medical Department Announcement for 1909-1910.” The capsule also held three June 15, 1910 newspapers. (Apparently that was a slow news day; one of the front page stories reported how a woman divorced her husband to marry his brother.)

At the gala, alumni got to see Freddie H. Fu, MD ’77, smiling ear to ear as he accepted the Philip S. Hench Distinguished Alumnus Award. (See story page 5.) Donald Leon, dean of the school from 1978 to 1984, was also there chatting with old colleagues and former students.

The PAA did brisk business that week. Three classes also met there for reunions.

Members of the CLASS OF ’40, brought together by Ed Brethauer, MD ’40, gathered at the school’s Senior Class Luncheon (held at the Twentieth Century Club on the 19th) and later for a small private dinner at the PAA on the 20th.

Gertrude Blumenschein, MD ’50, organized a weekend of reminiscence for the CLASS OF ’50 that included crashing the Alumni Dinner Dance. And later that week, Margaret Lally’s (MD ’85) efforts hooked up members of the CLASS OF ’85, on the evening of the 27th: same time, same place—but no band. It was only 15 years, not quite as much to dance about, Lally muses.

CLIFF’S NOTES: ANAL POWERS

Ahem. Scope and Scalpel productions traditionally provide a means for graduating classes to deconstruct the medical school experience and its attendant frustrations.

As such, the Class of 2000 borrowed from Mike Myers’s Bondian alter-ego, Austin Powers, to craft An‘al Powers and the Gunner Who Shagged Me. There’s not so much a plot here as there is a stream-of-consciousness series of flashbacks. The “storyline” centers on An‘al (pronounced An-‘alll) as the International Student of Mystery. Okay it doesn’t really center on anything, but it starts with An‘al as a recent grad, watching a television show recap his years of medical school. Key character development is laid during the poignant dance number “How to Get to Residency” (sung to the tune of “How to Get to Sesame Street”).

The actions of central characters, An‘al and fellow student Dr. Evil, who already has a PhD (world domination is her intended area of specialty), are less important than what they represent, which is essentially the struggle of Everyman to survive this grueling experience and reemerge, if not better, then bigger, into a new chapter of existence wherein “the license on the wall will be mine.”

Central to the exposition of this work are the repeated references to broadly drawn instructor-gurus. Each scene depicts yet another instance in which professors assert that theirs is the most important class in med school, whether the subject is cells or proctology, and further, they are the most important practitioners in their fields. Students attempt to gain favor while the improbability of these assertions becomes more and more apparent to them. It is by this means that the tension in the story builds.

Release finally comes in the Matching process, a vehicle designed to foreshadow the next life, where indeed, “We’ve done all to make ourselves docs for folks like you.” (Sung to the tune of “Mambo #5.”) –PMP
**ERNST KNOBIL**
**SEPTEMBER 20, 1926 – APRIL 13, 2000**

Ernst Knobil loved Alfa Romeos. He had three of them, and to feed the hunger of a bit of a lead foot, Knobil attended a racing school at the age of 51. Small wonder, then, that a man with such driving force went the distance in his life’s work.

For five decades, Knobil helped shape the field of neuroendocrinology. His work ultimately contributed to our understanding of the female reproductive system and is used today in assisted reproduction technology. Treatments for breast and prostate cancer also emerged from his findings.

The Cornell graduate taught at Harvard before coming to the University of Pittsburgh School of Medicine in 1961. Over the next 20 years, he built and chaired the Department of Physiology (now Cell Biology and Physiology), became its first Richard Beatty Mellon Professor, and founded the Center for Research in Reproductive Physiology.

Knobil moved on to the University of Texas-Houston in 1981 where he was dean of the medical school until 1984. The University of Texas appointed him the Ashbel Smith Professor for his lifetime of contributions to medicine and established a two-year postdoctoral research fellowship in his name. Through the years his accomplishments were recognized with numerous awards and honorary degrees. He received, for example, Pitt’s Dickson Prize in Medicine for work in neurobiology. And as recently as last year Knobil led an investigation of environmental toxins for the National Research Council.

Ernst Knobil died in Houston of pancreatic cancer on April 13.

—PMP

**IN MEMORIAM**

- **DANIEL ARENSBERG (MD ’70)**  
  March 9, 2000
- **LLOYD R. AXERS (MD ’35)**  
  August 1, 1999
- **HOWARD JEROME BERMAN (MD ’49)**  
  February 16, 2000
- **JOSE M. CANTELLOPS (MD ’48)**  
  January 30, 2000
- **JOHN I. DAVIS (MD ’47)**  
  December 19, 1999
- **GERALD A. ERHARD (MD ’40)**  
  November 3, 1999
- **LEE J. GOLDBLUM (MD ’80)**  
  March 20, 2000
- **ERNST KNOBIL (FACULTY)**  
  April 13, 2000
- **ROBERT L. LAMBERT (MD ’44)**  
  January 6, 2000
- **HARRY LEVIN (MD ’72)**  
  February 28, 2000
- **DAVID LOCKE (MD ’50)**  
  March 29, 2000
- **ANDREW JACK MCADAMS (MD ’35)**  
  December 25, 1999
- **CLAUDE W. MCKEE (MD ’37)**  
  February 20, 2000
- **WILLIAM MCKNIGHT (MD ’35)**  
  January 26, 2000
- **JOSEPH L. MORETTO (MD ’43)**  
  February 23, 2000
- **WILLIAM J. SEIFERTH (MD ’43)**  
  April 15, 2000
- **SAMUEL E. TISHERMAN (MD ’55)**  
  March 31, 2000
- **WILLIAM R. VOGAN (MD ’43)**  
  February 7, 2000
- **MURRY K. WEBER (MD ’54)**  
  January 26, 2000
- **PAUL F. WEBSTER (MD ’50)**  
  May 24, 1997
- **JOHN B. WERNING (MD ’60)**  
  November 29, 1999
- **CHARLES F. WHITAKER JR. (MD ’41)**  
  May 12, 1999
- **JAMES A. WILSON (MD ’46)**  
  September 12, 1999
- **HERMAN A. ZIEL (MD ’46)**  
  December 5, 1999

**WILLIAM K. MCKNIGHT, MD ’35**
**FEBRUARY 15, 1911 – JANUARY 26, 2000**

Although psychiatrist William McKnight certainly had a long, productive, and satisfying professional life, his widow Betty McKnight notes that his art probably gave him at least equal pleasure. Drawing, sketching, painting, really “anything and everything that took his fancy” ended up as a lifelong avocation. He would never sell any of his art, although he was frequently asked to, claiming shyly that he “wouldn’t know what to ask for it.”

Raised in the Pittsburgh area, McKnight ended up at the University of Pittsburgh for undergraduate as well as medical school. He entered the Army Medical Corps in 1941, was stationed at various bases in the United States and in the West Indies, and rose to the rank of lieutenant colonel. He also took postgraduate training at the Philadelphia Psychoanalytic Institute, held clinical and administrative positions at New York Hospital-Cornell Medical Center and the Connecticut State Department of Mental Health, and taught at Cornell University and the University of Pennsylvania—all before finally settling down in Arizona to retire at the age of 75 (this was his third attempt).

Betty McKnight remains at the retirement community in Green Valley where they made their home and where he was on the medical advisory committee. William McKnight’s art was finally formally presented at a show at Green Valley after he died, notes his wife, adding how secretly pleased he would have been.

—PMP
TAD CASSIDY: LEARNING RUSSIAN
BY SANDY TILNEY

Tad Cassidy (MD ’79) didn’t think twice.

When the University of Pittsburgh School of Medicine alumnus met visiting Russian physician Alexander Maltsev, something tugged at his heartstrings. During that meeting in 1992, Cassidy learned that Maltsev had used the same three catheters for years: Each time he needed one for a patient, he would rinse and boil it; this was the best he could do to sterilize. Then Maltsev told Cassidy how supplies were so scarce in Ulyanovsk, Russia, he would even pin his gloves to a line so they could dry and be used again later.

Maltsev didn’t need to say more. Cassidy bent down, opened a desk drawer, and handed him a Doppler machine.

“Here take this, I know we can get another one,” he assured Maltsev.

Then he hunted for some batteries. He also culled catheters from that day’s cases, along with any that had expired, figuring that those were certainly bound to be in better shape than the few Maltsev had relied on for years.

So began a friendship between the two radiologists.

After hearing of Maltsev’s plight, Cassidy felt compelled to do more. Cassidy, who is the chief of angiography and interventional radiology at Integris Baptist Medical Center in Oklahoma City, now works with a group of physicians from St. Luke’s Church in Oklahoma City. This group sponsored Maltsev’s initial trip, which was designed so that the Russian physician could learn about American techniques. The team now collects and sends supplies to Ulyanovsk. These days, Cassidy seems to be on an endless search for catheters, coronary balloons, and other equipment that isn’t readily available in Ulyanovsk. He stores them in his office, his garage, wherever he can find space, until it’s time for the next shipment. Once enough supplies are collected, Cassidy brings car loads of boxes to St. Luke’s where he and other physicians spend hours sorting, labeling, and packaging the equipment just so. Cassidy and his friends pay special attention to this mundane activity, and for good reason. A shipment worth more than $800,000 once sat in a Russian customs office for 18 months. Officials claimed the paperwork wasn’t completed correctly. Maltsev fought tirelessly to cut the red tape. Their reward after months of pleading and diplomacy: The supplies were burned because the “use by” dates had expired. But this pitfall only cemented Cassidy’s resolve.

Cassidy’s determination eventually placed him on a plane headed for Moscow. Again he was surrounded by packages. He toted as many supplies as he could fit in his bags, and prepared himself to teach Maltsev and other Russian physicians about Western procedures.

During his visit, Cassidy found himself doing a lot of the learning. He noticed that when Russians hear the word “hospital,” they become petrified. It’s understood that you go there to die. He was taught other lessons too. As he lectured on biliary drainage, which enables the liver to continue working in extremely critical cases but usually only prolongs life for maybe eight months, a hand immediately shot up.

Who can afford to have this done and why would you do this?

Cassidy thought the answer was obvious, but then realized what this audience member was really asking: If the procedure isn’t going to save a life, why would you bother putting a patient through the pain? And isn’t this a tremendous waste of resources?

It’s a fatalistic attitude, says Cassidy. The experience gave Cassidy a new perspective. He considers how few Americans appreciate or understand the larger forces—politics, value systems—that weigh into whether they will live or die.

Yet when he thinks of someone like Maltsev, someone with so little who is striving to do so much, Cassidy also is able to see how some forces can transcend continents. With his Russian friend, he shares a common goal: “I can’t change a health care system, but I can help one patient at a time.”
Another unsolved mystery. This bewildered young man was found in the 1963 *Hippocratean*, whose editors imply he is in a physiology lab. If you can fill us in on the details, you get a life subscription to *Pitt Med* and a Kewpie doll.